AF/1647

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of: Dan L. Eaton et al. **Group Art Unit: 1647**

Serial No.: 10/063,567 **Examiner: Rachel Kapust Hunnicutt**

Filed: May 2, 2002

For: Secreted and Transmembrane Polypeptides and Nucleic Acids Encoding the Same

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APPEAL BRIEF

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Dan L. Eaton et al. Serial No.: 10/063,567 Filed: May 2, 2002 For: *Secreted and Transmembrane Polypeptides and Nucleic Acids Encoding the Same*	Group Art Unit: 1647 Examiner: Rachel Kapust Hunnicutt Confirmation No.: 9763 Customer No.: 09157 **CERTIFICATE OF MAILING** I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on March 25, 2005 Teri Lee

APPEAL BRIEF

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

This Appeal Brief, filed in connection with the above captioned patent application, is responsive to the Final Office Action mailed on October 15, 2004. An Amendment in response to this Final Office Action and a Notice of Appeal was filed herein on October 29, 2004, which resulted in the Examiner issuing an Advisory Action on November 22, 2004.

Appellants hereby appeal to the Board of Patent Appeals and Interferences from the final rejection in this case. A request for an appropriate extension of time for the filing of this Appeal Brief is enclosed herewith.

The Commissioner is authorized to charge any fees which may be required, including extension fees, or credit any overpayment to Deposit Account No. 07-0630.

The following constitutes the Appellants Brief on Appeal.

I. REAL PARTY IN INTEREST

The real party in interest is Genentech, Inc., South San Francisco, California, by an assignment of the parent application Serial No. 10/006,867 recorded December 6, 2001, at Reel 012377 and Frame 0266.

II. RELATED APPEALS AND INTERFERENCES

The claims pending in the current application are directed to various forms of a polypeptide referred to herein as "PRO1291". There exist two related patent applications, (1) U.S. Serial No. 10/063,568, filed May 2, 2002 (containing claims directed to anti-PRO1291 polypeptide antibodies), and (2) U.S. Serial No. 10/063,703, filed May 8, 2002 (containing claims directed to nucleic acids encoding PRO1291 polypeptides). These two related applications are also under final rejection from the same Examiner and based upon the same outstanding rejection, wherein appeal of these final rejections are being pursued independently and concurrently herewith.

III. STATUS OF CLAIMS

The current application was originally filed with Claims 1-13. In an Amendment filed on August 5, 2004, Applicants canceled Claims 1-13 and added new Claims 14-16. Claims 14-16 remain pending and under final rejection, wherein the final rejection of those claims is being appealed herein.

IV. STATUS OF AMENDMENTS

No claim amendments were made subsequent to final rejection herein.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Independent Claim 14 is directed to various forms of an isolated polypeptide referred to in the present application as "PRO1291", a cell surface polypeptide that is shown for the first time in the present patent application to be (i) significantly overexpressed (or "upregulated") in human lung and esophageal tumors as compared to normal, non-cancerous human lung and esophageal tissue, respectively, and (ii) significantly underexpressed (or "downregulated") in human melanoma tumors as compared to normal, non-cancerous human skin tissue. More specifically, the various forms of the PRO1291 polypeptide recited in independent Claim 14 include, (i) the full-length PRO1291 polypeptide (amino acids 1-282 of SEQ ID NO:60), (ii) the full-length PRO1291 polypeptide lacking the cleaved signal sequence (amino acids 29-282 of SEQ ID NO:60), (iii) an isolated extracellular domain of the PRO1291 polypeptide (amino acids 1-257 of SEQ ID NO:60), (iv) the PRO1291 polypeptide encoded by the full-length encoding cDNA sequence disclosed as SEQ ID NO:59, and (v) the PRO1291 polypeptide encoded by the full-length cDNA deposited with the ATCC under ATCC Accession No. 209990. The amino acid sequence of the native "PRO1291" polypeptide (including the locations of all relevant domains such as the signal peptide and transmembrane domain) and the nucleic acid sequence encoding this polypeptide (referred to in the present application as "DNA59610-1556") are shown in the present specification as SEQ ID NOS:60 and 59, respectively.

Independent Claim 15 is directed to a chimeric polypeptide that comprises one of the polypeptides recited in independent Claim 14 which is fused to a heterologous polypeptide. Claim 16 depends from independent Claim 15. Specification support for each of Claims 14-16 can be found at least in the claims as originally filed.

VI. GROUNDS OF REJECTION TO BE REVIEWED UPON APPEAL

The grounds of rejection raised in the current appeal are twofold.

First, Claims 14-16 stand rejected under 35 U.S.C. § 101 as allegedly "not being supported by either a specific and substantial asserted or a well-established utility".

Secondly, Claims 14-16 stand rejected under 35 U.S.C. § 112, first paragraph, as the claimed invention is allegedly "not supported by a specific or substantial utility" and, therefore, the Examiner asserts that the specification fails to teach "how to use" the presently claimed invention.

VII. ARGUMENT

(1) Claims 14-16 stand rejected under 35 U.S.C. § 101 as allegedly "not being supported by either a specific and substantial asserted or a well-established utility"

Claims 14-16 stand rejected under 35 U.S.C. § 101 as allegedly not being supported by either a specific, substantial and credible asserted or a well-established utility. The sole basis for the Examiner's rejection is that the data presented in Example 18 of the present specification is insufficient under the present legal standards to establish a patentable utility under 35 U.S.C. § 101 for the presently claimed subject matter. Appellants strongly disagree and, therefore, respectfully traverse the rejection.

A. The Legal Standard For Utility Under 35 U.S.C. § 101

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001), an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility".

Under the Utility Guidelines, an asserted utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a particular composition of matter is useful in general as a diagnostic tool, without also identifying the particular condition that is to be diagnosed using that diagnostic tool. However, when the condition that is capable of being diagnosed is specifically identified and linked to the claimed subject matter, the asserted utility satisfies the "specificity" requirement.

The requirement of a "substantial" utility defines a "real world" use, and derives from the U.S. Supreme Court's holding in Brenner v. Manson, 383 U.S. 519, 534 (1966) stating that:

> "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility."

In explaining the "substantial" utility standard, the Manual of Patent Examining Procedure (MPEP) § 2107.01 cautions, however, that Patent Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient" (MPEP § 2107.01, emphasis supplied). Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement, set forth in MPEP § 2107 II(B)(1) gives the following instruction to patent examiners:

> "If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility". (Emphasis supplied).

Moreover, the Utility Guidelines make clear that the requirement for the asserted utility be "substantial" arises solely for the purpose of excluding:

> "'throw-away' or 'insubstantial'.....utilities, such as the use of a complex invention as landfill, as a way of satisfying the utility requirement of 35 U.S.C. § 101". (66 Fed. Reg. 1092, 1098 (2001), emphasis supplied).

Finally, the Utility Guidelines also restate the Patent Office's long established position that any asserted utility must be "credible". "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the applicant's assertions." (MPEP § 2107 II(B)(1)(ii)). According to the Revised Interim Utility Guidelines Training Materials published by the U.S. Patent Office in 1999 (a copy of which is attached herewith and labeled as "Evidentiary Exhibit A"), Office personnel must always accept a patent applicant's assertion of utility as "credible" unless (1) the logic underlying the

assertion is "seriously flawed", or (ii) if the facts upon which the assertion of utility is based are "inconsistent with the logic underlying the assertion".

Moreover, the U.S. Patent Office also sets forth the evidentiary standard as to utility rejections under 35 U.S.C. § 101. In general, an Applicant's assertion of utility creates a presumption of utility that is sufficient to satisfy the utility requirement of 35 U.S.C. § 101, "unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope." In re Langer, 503 F.2d 1380, 1391 (CCPA 1974). See, also In re Jolles, 628 F.2d 1322 (CCPA 1980); In re Irons, 340 F.2d 974 (CCPA 1965); In re Sichert, 566 F.2d 1154, 1159 (CCPA 1977). Compliance with 35 U.S.C. § 101 is a question of fact. Raytheon v. Roper, 724 F.2d 951, 956 (Fed. Cir. 1983) cert. denied, 469 U.S. 835 (1984). The evidentiary standard to be used throughout ex parte examination in setting forth a rejection is a preponderance of the totality of the evidence under consideration. In re Oetiker, 977 F.2d 1443, 1445 (Fed. Cir. 1992). Thus, to overcome the presumption of truth that an assertion of utility by the applicant enjoys, the Examiner must establish that it is more likely than not that one of ordinary skill in the art would doubt the truth of the statement of utility. Only after the Examiner makes a proper *prima facie* showing under this standard does the burden of rebuttal shift to the patent applicant.

B. The Data Supporting a Patentable Utility

The data presented by the Applicants in the present application and which underlies the current dispute is that which is presented in Example 18 starting on page 140 of the specification. Example 18 describes the results obtained using a very well-known and routinely employed polymerase chain reaction (PCR)-based assay which allows one to quantitatively measure the level of gene expression for any gene in any sample of mRNA or cDNA produced from that mRNA. Moreover, as described in Example 18, a β-actin control is employed to ensure that the total amount of nucleic acid in all samples being tested is the same. Since use of the β-actin control assures that all tested samples contain the same amount of total nucleic acid and since the assay allows one to quantitatively measure the amount of expression for any specific gene of interest, the assay allows one to make clear, concise and reproducible quantitative comparisons of "gene-specific" expression

between two or more samples. In other words, this well known and widely-employed assay allows one to detect quantitative differences in gene expression between two or more different samples. Therefore, using this assay, one can determine whether any gene of interest is expressed at a higher or lower rate in a sample derived from a first tissue of interest (say, for example, a cancerous tumor tissue) than in a second tissue of interest (say, for example, a normal tissue).

It is exactly this type of comparison that is presented in Example 18 for the PRO1291 polypeptide-encoding nucleotide sequence referred to in the present specification as DNA59610-1556. More specifically, the data in Example 18 demonstrate that there is a quantitatively detectable difference in DNA59610-1556 expression in:

(a) at least one type of cancerous human lung tumor when compared to its normal, non-cancerous human lung tissue counterpart (detectably higher expression in the tumor than in the corresponding normal tissue);

(b) at least one type of cancerous human esophageal tumor when compared to its normal, non-cancerous human esophageal tissue counterpart (detectably higher expression in the tumor than in the corresponding normal tissue); and

(c) at least one type of cancerous human melanoma skin tumor when compared to its normal, non-cancerous human skin tissue counterpart (detectably lower expression in the tumor than in the corresponding normal tissue).

Based upon these data, Applicants have asserted in the present patent application that this reproducible, quantitative difference in the level of expression of DNA59610-1556 can be exploited for diagnosing the presence of particular types of lung, esophageal and/or melanoma tumors in a human subject who is suspected of having such a tumor. More specific to the presently claimed invention, the polypeptides claimed herein find use as immunogens useful for the preparation of antibodies that can be employed as diagnostic tools for measuring the level of expression of the PRO1291 polypeptide in a tissue sample of unknown pathology, thereby assisting in the determination of the presence of certain types of human lung, esophageal and melanoma tumors.

Contrary to the Applicants assertion of utility herein, however, the Examiner alleges that the differential gene expression described in Example 18 does not render the presently claimed polypeptides patentably useful. Applicants respectfully submit, however, that upon application of the appropriate legal standards described above, the proper conclusion is that the present application does, in fact, disclose a patentable utility for the claimed invention.

C. Legal Analysis of the Data and the Assertion of a Patentable Utility

Applicants respectfully submit that the data presented in Example 18 of the specification support a "specific, substantial and credible" utility for the presently claimed invention.

(i) The Requirement For A "Specific" Utility

The first requirement as set forth in the above described Utility Guidelines is that an asserted utility for a claimed invention must be "specific". In other words, the asserted use for the claimed invention must be identified with specificity and that use must be specifically linked to the subject matter of the claimed invention.

As described above, Applicants have clearly demonstrated that the PRO1291 polypeptide of SEQ ID NO:60 is detectably overexpressed in certain cancerous human lung and esophageal tumors as compared to normal, non-cancerous human lung and esophageal tissue, respectively. Moreover, Applicants have clearly demonstrated that the PRO1291 polypeptide of SEQ ID NO:60 is detectably underexpressed in at least one type of cancerous human melanoma tumor as compared to its normal, non-cancerous counterpart skin tissue. As such, one or ordinary skill in the art can readily see that anti-PRO1291 antibodies would be quite useful as diagnostic tools for detecting the differential expression of the gene encoding the PRO1291 polypeptide in human tissues of unknown pathology, wherein such antibodies can be readily produced using any of the presently claims PRO1291 polypeptides as an immunogen. Such a use, in turn, provides valuable diagnostic information for determining the presence of (i) human lung and esophageal tumors that overexpress the PRO1291 polypeptide relative to normal human lung or esophageal tissue, respectively, or (ii) melanoma tumors that underexpress the PRO1291 polypeptide relative to the normal counterpart human tissue.

Certainly, therefore, the utility asserted for the presently claimed subject matter is described with "specificity".

> In the Final Office Action mailed herein on October 15, 2004, however, the Examiner asserts:
>
> "[t]issue-specific expression such as that found in Example 18 is not specific to the polynucleotide [encoding the polypeptide of SEQ ID NO:60]. It does not depend on any characteristic of the nucleic acid molecule itself." (see the Final Office Action at page 4, lines 6-7, emphasis supplied).

Applicants simply fail to understand the Examiner's point and believe it to be nonsensical. The differential gene expression profile presented in Example 18 for DNA59610-1556 (i.e., PRO1291) is an important characteristic of that molecule, is specific for that molecule and depends from that molecule. As described above, the "specificity" requirement for an asserted utility under 35 U.S.C. § 101 merely requires a patent applicant to set forth and describe the asserted utility with specificity. Applicants have herein asserted that the claimed invention is useful diagnostically and has also specifically identified and described the diseases for which the invention is diagnostically useful. Therefore, Applicants respectfully submit that this is clearly sufficient to satisfy the "specificty" requirement.

(ii) The Requirement For A "Substantial" Utility

As described above, the second requirement set forth in the Utility Guidelines is that an asserted utility for a claimed invention must be "substantial", meaning that the claimed invention must serve a "practical purpose" (see MPEP § 2107 II(B)(1)) which is not a "throw-away or insubstantial [use], such as the use of a complex invention as landfill. (66 Fed. Reg. 1092, 1098 (2001), emphasis supplied).

In this regard, Applicants first note that in the Advisory Action mailed herein on November 22, 2004, the Examiner states:

> "Applicants argue that Example 18 enables one of skill in the art to quantitatively measure the difference in expression of DNA59610-1556 in at least one type of human lung tumor, human esophageal tumor, and/or human melanoma skin tumor when compared to the corresponding normal tissue. Applicants argue that the utility of the claimed polypeptides is that they can be used as diagnostic tools for the detection and diagnosis of certain types of lung, esophageal, and melanoma tumors. This is not a substantial utility." (Emphasis supplied).

In essence, therefore, the Examiner's argument is that having the ability to diagnose the presence of a particular type of cancer in a human subject who is suspected or at risk of having that particular type of cancer is (i) "impractical", (ii) a "throw-away" use which is akin to the use of "a complex invention as a landfill", and (3) "insubstantial". Applicants respectfully submit that nothing could be farther from the truth. It is well known that common human cancers such as lung, esophageal and melanoma cancer result in the death of many countless thousands of people each year. Scientific and medical researchers spend millions of dollars each year in efforts to develop new, useful ways of treating and diagnosing the presence of these types of cancer in humans, and each year, such efforts make strides forward in reducing the overall mortality rate as a result of these types of cancer.

As described above, Applicants have herein for the first time identified a particular human gene that is differentially expressed in certain types of cancerous human lung, esophageal and melanoma tumors as compared to their normal, non-cancerous counterpart tissues. This discovery provides for the first time the ability to exploit this previously unknown differential gene expression pattern for the purpose of determining whether a particular human lung, esophageal or skin tissue sample of previously unknown pathology is (or is not) cancerous. Antibodies that can be produced and characterized using the presently claimed polypeptides may be employed for just such diagnostic testing. Arguing that such a use is "not substantial" is simply untenable. As such, Applicants submit that the utility presently asserted for the claimed invention meets the "substantiality" requirement set forth by the Utility Guidelines and required by the U.S. Supreme Court in Brenner v. Manson, 383 U.S. 519 (1966).

As a final note, now that Applicants have identified and described in the present application the differential expression pattern of the PRO1291 polypeptide in certain human cancers as compared to their respective normal tissues, antibodies that can be produced and characterized using the presently claimed polypeptides as immunogens could be used even today for useful diagnostic purposes (i.e., the utility is "currently available"). Such certainly, however, is not required to satisfy the requirement for "substantiality". As indicated above, MPEP § 2107.01 cautions that Patent Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient" (MPEP § 2107.01, emphasis supplied).

(iii) The Requirement For A "Credible" Utility

The final requirement set forth in the Utility Guidelines is that an asserted utility for a claimed invention must be "credible". As described above and as set forth in Evidentiary Exhibit A, Office personnel must always accept a patent applicant's assertion of utility as "credible" unless (i) the logic underlying the assertion is "seriously flawed", or (ii) if the facts upon which the assertion of utility is based are "inconsistent with the logic underlying the assertion". Based upon this standard, Applicants respectfully submit that the Examiner herein is required to accept the asserted utility herein as credible.

In this regard, the Examiner in the Final Office Action mailed on October 15, 2004 asserts:

> "[i]n Example 18, the specification merely states that the gene is 'more highly expressed' in one tissue as compared to another. There is no guidance in the specification as to how high the levels are.....[t]he only thing Applicants teach is that the gene was 'more highly expressed', and this does not enable the skilled artisan to differentiate amongst expression levels in order to diagnose any diseases." (see the Final Office Action at page 4, lines 11-21, emphasis supplied).

Applicants strongly disagree. The two important aspects about the data presented in Example 18 are (1) there is a detectable difference in DNA59610-1556 gene expression between the various tumor samples tested and their normal respective counterparts, and (2) the level of expression of DNA59610-1556 is detectably higher in the human lung and esophageal tumors tested than in the corresponding normal human lung and esophageal tissues, respectively, and detectably lower in the human melanoma tumors tested then in the corresponding normal human skin tissues. The Examiner seems to focus on "how much higher" or "how much lower" (i.e., requiring Applicants to provide exact numbers), but Applicants submit that this is not relevant to the issue at hand, nor is it required for the claimed invention to be useful. What is important for the diagnostic utility asserted in the present application is (i) to be able to quantitatively compare the level of DNA59610-1556 expression in a tumor sample to a normal sample and (2) to detect a relative difference in the level of gene expression between the tumor and normal samples. The exact magnitude or size of that difference is irrelevant to the utility.

For example, the asserted utility relies only upon being able to detect a relative difference in the level of DNA59610-1556 expression in the tumor sample as compared to the normal sample...the exact magnitude thereof is not relevant. Thus, if one employs the described assay to quantitatively compare the level of DNA59610-1556 expression in, for example, (i) an human esophagus-derived tissue sample of unknown pathology and (ii) a corresponding normal human esophageal tissue sample, one of two results will be obtained. First, the investigator may find that the level of DNA59610-1556 expression in the unknown sample as compared to the known normal sample is either the same or detectably lower. In this case, no useful diagnostic information is obtained. However, if the investigator finds that the level of DNA59610-1556 expression is detectably higher in the sample of unknown pathology as compared to known normal sample, then useful diagnostic information is obtained. Therefore, contrary to the Examiner assertion quoted above, knowledge of the fact that DNA59610-1556 is "more highly expressed" in one tissue as compared to another does "enable the skilled artisan to differentiate amongst expression levels" and, as such, does provide useful diagnostic information.

The Examiner next asserts:

> "Applicants have not taught baseline levels of expression, nor have Applicants provided numerical values for the levels of overexpression and underexpression." (see the Advisory Action mailed on November 22, 2004).

Applicants agree with this statement. No actual numerical values are provided. Applicants also submit, however, that the asserted utility is not in any way dependent upon the measurement or determination of "actual numerical values" for the level of gene expression (e.g., copy number of PRO1291 polypeptides per cell, or the like). As described above, the diagnostic assay described herein is a comparative one, meaning that the utility is based upon a relative comparison of expression levels between (i) a known normal tissue sample (which is, by the way, the baseline level of expression referred to by the Examiner above) and (ii) a tissue sample of unknown pathology. Useful diagnostic information is obtained when a relative difference is observed. All that is important to the utility is that a relative difference is (or is not) observed. Determining the exact numerical value of that difference is irrelevant.

For example, when a scientific researcher uses an antibody in a standard Western Blot analysis to measure the level of expression of a polypeptide in two different samples, he or she can determine whether there is a relative difference in expression levels between the two samples simply by comparing the relative intensities of the radioactive signal provided by each test sample. Clearly the determination of the presence of a relative difference in expression levels (which, as described above, provides useful diagnostic information) is independent of actually calculating numerical values in terms of polypeptide copy number per cell, or the like. It is the observation of a relative difference between a test sample and a normal sample that is important to the asserted utility, not a calculation of the exact numerical magnitude of that difference.

In support of the outstanding rejection, the Examiner next asserts:

> "[t]here is no information in the specification as to the type of tumors, malignant or benign, that are affected. Applicants do not provide any evidence that indicates....whether the results were statistically significant. Applicants have provided no indication of the nature of the number of samples that were used. The art teaches that individual changes may be associated with clonal expansion, which would not be characteristic of the class of tumors as a whole (see, for example, Bover et al., 1998, Cell. Mol. Biol. 44(3):493-504)." (see Final Office Action at page 4, lines 13-19).

In response, Applicants first wish to point out that the Examiner is making an incorrect assumption about what Applicants are claiming as utility for the claimed invention. It appears that the Examiner believes that Applicants are claiming that the observed and herein described differential expression profile of DNA59610-1556 is diagnostic for all lung, esophageal and melanoma tumors. In fact, this is clear in that the Examiner focuses on things such as "what types of tumors were tested", "how many tumors were tested" and "were the numbers sufficiently high to provide statistically significant results", etc. This assumption, however, is patently incorrect. Applicants do not in any way assert that the observed and herein described differential expression profile of DNA59610-1556 is diagnostic for all lung, esophageal and melanoma tumors. In fact, Applicants are unaware of the existence of any diagnostic test that is capable of doing that. To the contrary, Applicants merely claim that the observed and herein described differential expression profile of DNA59610-1556 is diagnostic for the presence of (i) only those lung and esophageal tumors that exhibit detectable overexpression of DNA59610-1556 as compared to the corresponding and respective normal tissue type and (ii) only those melanoma tumors that exhibit detectable underexpression of DNA59610-1556 as compared to the corresponding normal tissue type. This provides a clear and currently available benefit to the public.

For example and for purposes of clarification, it is clear that the data presented in Example 18 and described above demonstrates that the expression of DNA59610-1556 is upregulated in at least one type of lung tumor and at least one type of esophageal tumor as compared to the normal corresponding tissue. As such, as described above, an investigator may employ the assay described in Example 18 to quantitatively compare the level of DNA59610-1556 expression in, for example, (i) a human esophageal-derived tissue sample of unknown pathology, but which is suspected of being

an esophageal tumor, and (ii) a known normal human esophageal tissue sample. If the investigator finds that the levels of DNA59610-1556 expression in the two tissue samples are not detectably different, then that information is not diagnostically useful. On the other hand, however, if the investigator finds that the level of DNA59610-1556 is detectably and reproducibly higher in the sample of unknown pathology as compared to the sample of normal pathology, then useful diagnostic information is clearly obtained. Since Applicants are not asserting a "general" diagnostic utility for the entire class of all human lung tumors, or all human esophageal tumors, or all human melanoma tumors, there is no need to test and provide data for numerous different types of human lung, esophageal or melanoma tumors, nor is there a need to demonstrate "statistical significance" across a wide range of different tumor types. As such, a currently existing benefit to the public does exist.

The Examiner next asserts:

> "[o]ne skilled in the art would not know whether the gene is actually more highly expressed in certain tumors or whether the 'overexpression' is due to aneuploidy which occurs frequently in cancer." (see the Advisory Action mailed on November 22, 2004).

This argument is completely irrelevant to the issue at hand. Clearly, it doesn't matter at all why there is overexpression in the tumor sample as compared to the normal sample or what serves as the mechanism that results in this observed overexpression. The overexpression observed in the tumor may be a result of aneuploidy as suggested by the Examiner, or it may be a result of some other unknown phenomenon. The utility asserted herein is based upon the ability to use the present invention in such a way so as to detect differential expression between two tissue samples. The mechanism by which that differential expression occurs is simply irrelevant to the asserted utility.

As a final note, Applicants wish to comments on the Bover et al. article cited by the Examiner in the Final Office Action mailed on October 15, 2005. The Examiner's reliance on this article for support of the outstanding rejection clearly demonstrates a serious lack of understanding of the claimed invention and the data that supports a patentable utility therefor. The Bover et al. article merely teaches that alterations in the level of gene amplification at the genomic DNA level may occur during clonal expansion of cells that are originally derived from a primary tumor, for

example, when those cells are expanded through multiple generations of growth *in vitro*. These teachings are completely irrelevant to the issue at hand as the above described diagnostic utility has nothing to do with detecting amplification of segments of genomic DNA. To the contrary, the herein asserted utility is based upon the ability to measure gene expression at the mRNA or protein level. Moreover, as described in Example 18, the samples being tested are derived from primary human tumors and, as such, anything that happens to cells originally derived from primary tumors when they are propagated through multiple generations of growth *in vitro* is completely irrelevant to the issue at hand.

Given all of the above, Applicants respectfully submit that the assertion of utility herein is "credible" in that (i) the logic underlying the assertion is not "seriously flawed", nor (ii) the facts upon which the assertion of utility is based are not "inconsistent with the logic underlying the assertion".

In summary, therefore, the utility asserted herein is "specific" in that it describes a clear diagnostic utility and furthermore describes the specific disease conditions associated with that utility, i.e., those human lung, esophageal and melanoma tumors exhibiting aberrant expression of the PRO1291 polypeptide as compared to normal. Moreover, the utility asserted herein is "substantial" in that it provides a "currently available benefit to the public". In this regard, as described above, the legal standards for utility under 35 U.S.C. § 101 require that "any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a 'substantial' utility'" (see, M.P.E.P. § 2107.01, emphasis supplied). Finally, the utility asserted herein is "credible" in that the data presented in Example 18 of the current specification clearly shows that the PRO1291 polypeptide is (i) detectably upregulated in at least one type of cancerous human lung and esophageal tumor when compared to the corresponding and respective normal, non-cancerous tissue, and (ii) detectably downregulated in at least one type of cancerous human melanoma tumor when compared to the corresponding normal, non-cancerous skin tissue. Thus, while the data presented in the present application and described in detail herein may not necessarily provide a diagnostic test for the presence or absence of all lung-, esophageal- and melanoma-derived tumors (in fact, Applicants

believe that such a test may not ever exist), it does provide a diagnostic test for at least a subset of those.....and that is all that is required to satisfy the requirements of 35 U.S.C. § 101. It is respectfully submitted, therefore, that the outstanding rejection under 35 U.S.C. § 101 is improper and Applicants respectfully request reversal of this rejection.

(2) **Claims 14-16 stand rejected under 35 U.S.C. § 101 as allegedly "not being supported by either a specific and substantial asserted or a well-established utility"**

Claims 14-16 stand rejected under 35 U.S.C. § 112, first paragraph, as the claimed invention is allegedly not supported by a specific or substantial utility and, therefore, the Examiner asserts that the specification fails to teach "how to use" the invention as claimed. Applicants respectfully traverse the rejection.

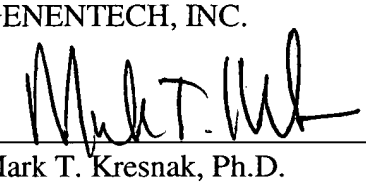
In this regard, Applicants refer to the arguments and information presented above in response to the outstanding rejection under 35 U.S.C. § 101, wherein those arguments are incorporated by reference herein. Applicants respectfully submit that as described above, the presently claimed invention is supported by a specific, substantial and credible utility and, therefore, the present specification teaches one of ordinary skill in the art "how to use" the claimed invention without undue experimentation, as described above. Specifically, as described herein and in the current specification As such, Applicants respectfully request reconsideration and reversal of the outstanding final rejection of Claims 14-16.

VIII. CONCLUSIONS

For the reasons given above, Applicants respectfully submit that the present specification clearly describes, details and provides a patentable utility for the claimed invention. Moreover, it is respectfully submitted that based upon this disclosed patentable utility, the present specification clearly teaches "how to use" the presently claimed antibody. As such, Applicants respectfully request reconsideration and reversal of the outstanding rejections of Claims 1-5.

Respectfully submitted,

GENENTECH, INC.

By: 

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CLAIM APPENDIX

14. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) amino acids 1-282 of SEQ ID NO:60;

(b) amino acids 29-282 of SEQ ID NO:60;

(c) amino acids 1-257 of SEQ ID NO:60;

(d) the amino acid sequence encoded by the full-length coding sequence of SEQ ID NO:59; and

(e) the amino acid sequence encoded by the full-length coding sequence of the cDNA deposited with the ATCC under ATCC accession no. 209990.

15. A chimeric polypeptide comprising a polypeptide according to Claim 14 fused to a heterologous polypeptide.

16. The chimeric polypeptide of Claim 15, wherein said heterologous polypeptide is an epitope tag or an Fc region of an immunoglobulin.

Evidentiary Exhibit A

REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS

Contents

SYNOPSIS OF APPLICATION OF THE REVISED INTERIM UTILITY GUIDELINES

It is assumed at this point in the analysis that the specification has been reviewed and an appropriate search of the claimed subject matter has been conducted. It is also assumed that some "utility" is disclosed in the specification or is recognized to be well-established in the art. The examiner should determine whether any asserted utility is specific and substantial, and if so, determine whether such asserted utility is credible. In determining credibility the examiner should consider whether or not there currently are similar or equivalent materials and/or procedures available for achieving that utility. If there are, the utility is credible and no rejection under 35 U.S.C. § 101 should be made.

Guidance for Various Examination Situations

I) a) For method claims that recite more than one utility, if at least one utility is credible, specific, and substantial, a rejection under 35 U.S.C. § 101 should not be made. If any utility in such a claim is not a specific and substantial credible utility, i.e., the claim encompasses at least one utility that does not meet the requirements of 35 U.S.C. §101, the rejection of the claim should be addressed under 35 U.S.C. § 112, first paragraph, scope of enablement.

b) For product claims that do not recite any utilities, disclosure or assertion of one specific, substantial and credible utility meets the criteria of 35 U.S.C. § 101.

II) If no credible, specific, and substantial utility is asserted in the specification and none is well established, a rejection under 35 U.S.C. § 101 would be proper.

III) Cure or prevention - Utilities that constitute curing or preventing a condition are sometimes not credible to one of skill in the art and thus may raise a question under 35 U.S.C. § 101. However, any rejection based on lack of credible utility must be supported by documentary evidence or sound technical reasoning.

IV) Treatment - Since most diseases or conditions can be treated, rejections under 35 U.S.C. § 101 for treatment claims should rarely be made.

V) Vaccines - Since vaccines are regularly prepared to combat various viruses and organisms, vaccines would have a credible utility to one of skill in the art. Thus, vaccines, including those for small pox, should not raise a question under 35 U.S.C. § 101.

VI) Materials to be used for research, or methods of using those materials for research, raise issues of whether the utilities require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. See, e.g., Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966) wherein a research utility was not considered a "substantial utility."

Definitions

"Credible utility" – Where an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being "wrong". Rather, Office personnel must determine if the assertion of utility is credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. A *credible* utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use. For example, no perpetual motion machines would be considered to be currently available. However, nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers. Therefore, the credibility of such an assertion would not be questioned, although such a use might fail the *specific* and *substantial* tests (see below).

"Specific utility" – A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as

diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (**Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. § 101.**)

C. A method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

D. A method of making a material that itself has no specific, substantial and credible utility.

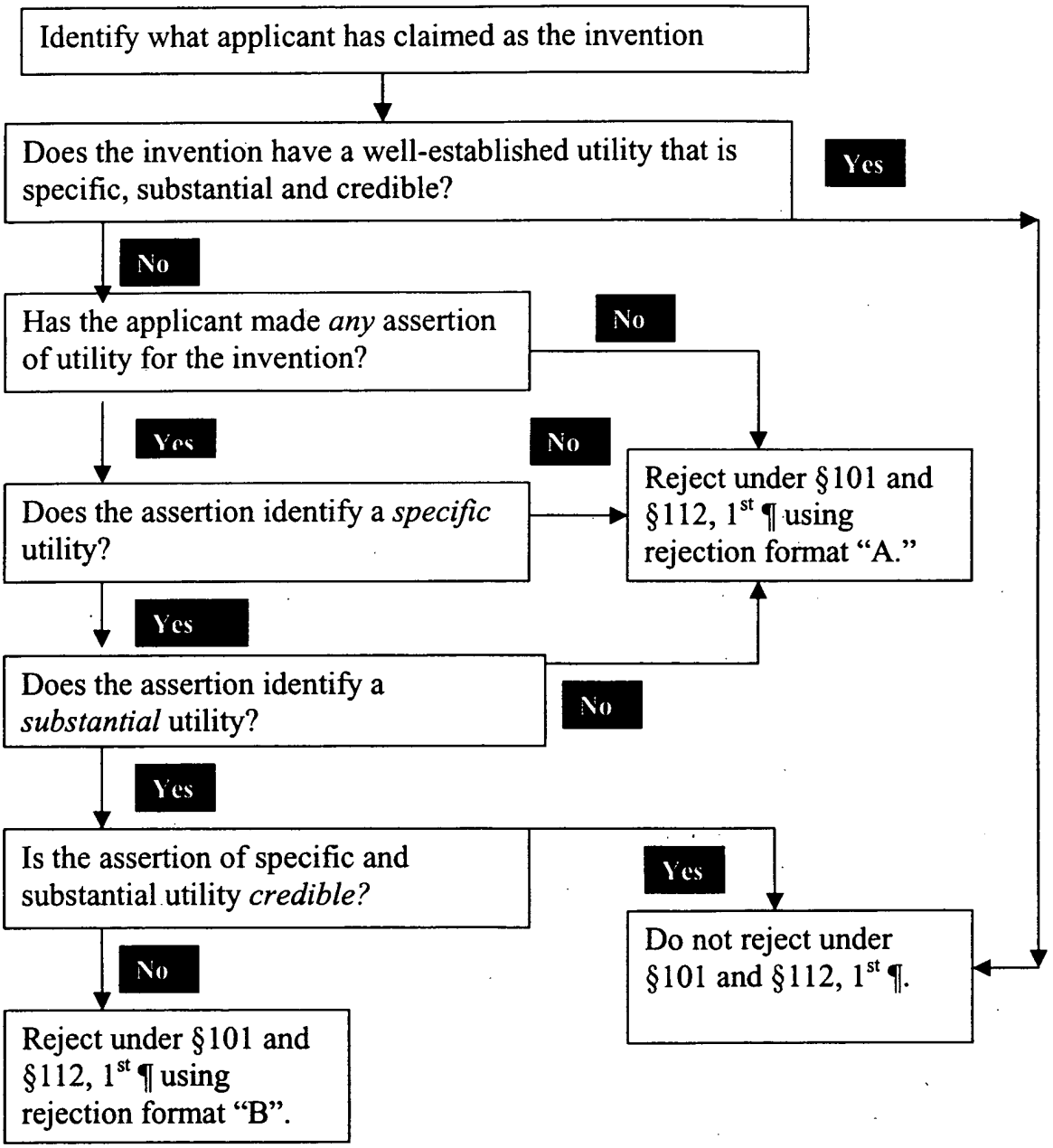
E. A claim to an intermediate product for use in making a final product that has no specific, substantial and credible utility.

Note that "throw away" utilities do not meet the tests for a *specific* or *substantial* utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C. §101. This analysis should, of course, be tempered by consideration of the context and nature of the invention. For example, if a transgenic mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial *asserted* utility would be considered to be met.

"Well established utility" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a nonspecific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA. If this were the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as landfill, an amusement device, a toy, or a paper weight; any carbon containing molecule would have a "well established utility" as a fuel since it can be burned; and any protein would

have well established utility as a protein supplement for animal food. This is not the intention of the statute.

Utility Review Flowchart



Rejection format "A": **Applicant has not disclosed any specific and substantial utility for the claimed invention, credibility will not be assessed.**

Rejection format "B": **Applicant has disclosed at least one specific and substantial utility for the claimed invention, but the assertion is not credible.**

Form Paragraph

7.05.01 - UTILITY REJECTIONS UNDER 35 U.S.C. § 101 AND 35 U.S.C. 112, FIRST PARAGRAPH

Claim [1] rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a [2] asserted utility or a well-established utility.

[3]

Claim [4] also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a [5] asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Format A: No specific and substantial utility

a) Insert the same claim numbers in brackets 1 and 4.

b) Insert "specific and substantial" in brackets 2 and 5.

c) In bracket 3, insert the explanation as to why the claimed invention is not supported by a specific and substantial asserted utility or a well-established utility. Note in the office action that credibility will not be assessed.

d) Format A is to be used either when there is no asserted utility or when there is an asserted utility that is not specific and substantial.

Format B: No credible utility

a) Insert the same claim numbers in brackets 1 and 4.

b) Insert "credible" in brackets 2 and 5.

c) In bracket 3, insert the explanation as to why the claimed invention is not supported by either a credible asserted utility or a well-established utility. Note that a utility that is inoperative is not credible.

Format C: For claims that have multiple utilities, some of which are not specific and/or substantial, and some of which are not credible, but none of which are specific, substantial and credible:

a) Insert the same claim numbers in brackets 1 and 4.

b) Insert "specific and substantial asserted utility, a credible" in brackets 2 and 5.

c) In bracket 3, insert the explanation as to why the claimed invention is not supported by a specific and substantial asserted

utility, a credible asserted utility or a well-established utility. Each utility should be addressed.

UTILITY GUIDELINES: TRAINING EXAMPLES

Example 1: Alternative Uses Claimed

Specification: The specification relates to the prevention and treatment of microbe X infection, a common infection, by administering compound A.

Claim:

1. A method for preventing or treating microbe X infection comprising administering to an animal in need thereof an effective amount of compound A.

2. A method for preventing microbe X infection comprising administering to an animal in need thereof an effective amount of compound A.

Analysis: The following analysis includes the questions that need to be asked according to the guidelines and the answers to those questions based on the above facts:

1) Based on the record, is there a "well established utility" for the claimed invention? Since each claim is directed to a specific method of use, the utility of each of these claims is limited to that use and the examiner should not look to a "well established utility" for the composition used in the claimed method. Consequently, the answer to the question is no.

2) Has the applicant made any assertion of utility for the specifically claimed invention? Yes. In fact, for claim 1 there are two asserted utilities, i.e., preventing microbe X infection and treating microbe X infection. Since there are two asserted utilities for claim 1, each must be analyzed. For claim 2, the utility is preventing microbe X infection.

3) Is the asserted utility specific? Since microbe X infection is a known infection, and the treatment claimed is directed to a *particular* combination of treatment and agent, the utilities of preventing or treating the infection define specific and particular uses, and are therefore specific utilities.

4) Is the asserted utility substantial? The characterization of the disease as a common infection establishes the presumption that the asserted utilities have a "real world" context. Therefore, the asserted utility is substantial.

5) Is the asserted specific and substantial utility credible? Since infections are conventionally treatable, the answer to this question would be yes regarding the treatment of microbe X infection. However, the claims also recite preventing microbe X infection. The broadest reasonable interpretation of the term infection merely requires that one microorganism gain entry into the cells of a host. It is known in the art that the activity of microbe X is similar to the activity of microbe Y which is known to enter the cells of a host through various pathways. Based on this similarity, it is presumed that microbe X can gain entry into the cells of a host through a multitude of avenues. There is no evidence in the specification or of record which demonstrates that preventing entry via all such avenues is credible, and therefore that utility would not be

credible and a rejection of claims 1 and 2 under 35 U.S.C. § 101/112, first paragraph, would be reasonable with respect to this utility.

Thus, the conclusion of this analysis for claim 1 is that the treatment of microbe X infection meets the criteria for a specific, substantial, and credible utility whereas the prevention of microbe X infection is not a credible utility. No rejection under 35 U.S.C. § 101 should be made against claim 1. The presence of the utility that is not credible in claim 1 (preventing microbe X infection) should be addressed in a rejection under 35 U.S.C. §112, first paragraph, scope of enablement. With respect to claim 2, both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should be made since the prevention utility is not credible.

Examiner's Rejection of claim 2

Claim 2 is rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a credible asserted utility or a well-established utility. Specifically, claim 2 is directed to a method of preventing microbe X infection. However, the term "infection", given its broadest reasonable interpretation consistent with the specification, merely requires that one microorganism gain entry into the cells of a host. It is known in the art that the activity of microbe X is similar to the activity of microbe Y which is known to enter the cells of a host. Based on this similarity, it is presumed that microbe X can gain entry to the cells of a host through a multitude of avenues. There is no evidence in the specification or of record which demonstrates that preventing entry via all such avenues is credible, and therefore that utility is not credible. Furthermore, since the claim is directed to a method, the utility analysis is limited to that recited

method. Claim 2 is also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it will operate as intended without undue experimentation.

Attorney Arguments with Evidence (Alternative I)

Claim 2 has been rejected by the examiner under 35 U.S.C. § 101 and 35 U.S.C. 112, ¶1. The examiner asserts that a credible utility has not been disclosed. Reconsideration under 37 CFR 1.111 is requested.

In support of applicants' statement of utility, attached hereto is an opinion declaration under 37 CFR 1.132 by an expert in the art (see In re Alton, 76 F.3d 1168, 37 USPQ2d 1578 (Fed. Cir. 1996)) who states that it is known that microbe X only gains entry into the cells of a host through the mucosa in the nose and mouth. The expert goes on to say that administering compound A blocks the mechanism by which microbe X enters the cells of the mucosa thereby preventing infection by the microbe. The only reasonable conclusion that could be reached based on the declaration and the fact that the statements made by the examiner are unsupported by evidence to the contrary is that preventing microbe X infection is, in fact, credible. For these reasons, the utility rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, should be withdrawn.

Examiner's Response to Attorney Arguments with Evidence (Alternative I)

If the examiner has no additional documentation to support the argument that microbe X gains entry into the cells of a host through a multitude of avenues so as to rebut the opinion declaration, the examiner should withdraw the utility rejections.

Attorney Arguments with Evidence (Alternative II)

Claim 2 has been rejected by the examiner under 35 U.S.C. § 101 and 35 U.S.C. § 112, ¶1. The examiner asserts that a credible utility has not been disclosed. Reconsideration under 37 CFR 1.111 is requested.

In support of applicants' statement of utility, attached hereto is a factual declaration under 37 CFR 1.132 by an expert with examples that unequivocally show that microbe X only gains entry into the cells of a host through the mucosa in the nose and mouth. The declaration also demonstrates that administering compound A blocks the mechanism by which microbe X enters the cells of the mucosa thereby preventing infection by the microbe. The only reasonable conclusion that could be reached based on the declaration and the fact that the statements made by the examiner are unsupported by evidence to the contrary is that preventing microbe X infection is, in fact, credible. For these reasons, the utility rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, should be withdrawn.

Examiner's Response to Attorney Arguments with Evidence (Alternative II)

The examiner should withdraw the utility rejections.

Example 2: Prevention

Specification: The specification relates to prevention or retardation of aging by administering an effective amount of compound A.

Claims:

1. A method for preventing aging comprising administering to a patient in need thereof an effective amount of compound A.

2. A method for retarding the aging process comprising administering to a patient in need thereof an effective amount of compound A.

Analysis: The following analysis includes the questions that need to be asked according to the guidelines and the answers to those questions based on the above facts:

1. Based on the record, is there a "well established utility" for the claimed invention? Since each claim is directed to specific method of use, the utility of each claim is limited to that use and the examiner should not look to a "well established utility" for the composition used in the claimed method. Consequently, the answer to the question is no.

2. Has the applicant made any assertion of utility for the specifically claimed invention? The answer is yes, i.e., a method for preventing or retarding aging.

3. Is the asserted utility specific? The method of using compound A requires the particular application of a single particular compound to be used in the claimed method. Therefore, the utility is specific.

4. Is the asserted utility substantial? Both preventing and retarding aging clearly define a "real world" context of use and, therefore, are substantial utilities.

5. Is the asserted "specific and substantial utility" credible? Since no material has been found to date which has been shown to or would be expected to prevent or retard aging and there are no working examples or other evidence in the record which would provide credibility to these claims it would be reasonable to conclude that the utility would not be credible based on the record.

Thus, the conclusion from this analysis is that both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should be made.

Note, had there been an indication in the specification that applicant's invention is the treatment of symptoms associated with aging, such as skin wrinkles, then the rejection could be avoided if claims are amended to clearly state treatment of symptoms or effects of aging.

Examiner's Rejection

Claims 1 and 2 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a credible asserted utility or a well-established utility.

The broadest reasonable interpretation of the claims in this situation is prevention of the aging process. In this rejection it is presumed that applicants intend to prevent or retard physiological aging and not

chronological aging, since the latter reads on the stoppage of time, which is contrary to the laws of nature and therefore not credible. The preventing or retarding of aging via systemic treatment is itself not credible on its face in view of contemporary knowledge in the art. No compound is currently known which would have these effects.

Physiological aging is a multi-faceted process which does not involve a single chemical or biological effect. Various theories have been propounded (see Lehninger et al., pages 341, 344, and 886 and Scandalios, pages 40 and 41) including (1) loss of telomerase activity and the relationship of telomere length to cell death, (2) accumulation of DNA mutations, and (3) temporal genes which regulate the output of structural genes. In view of these theories, one skilled in the art would conclude that the diverse aspects of aging, e.g. loss of muscle tone, slowing of metabolism, graying of hair, etc. operate via different mechanisms. There is no reason why one skilled in the art would expect a single compound to prevent or retard all of these diverse aspects.

Heretofore the art has recognized only the topical treatment of the external manifestations of aging, e.g., skin wrinkling, as an anti-aging utility (see U.S. Patent No. 5,340,568, for example). Note that skin wrinkling is but a single manifestation of the general process of aging.

Furthermore, since the claims are directed to methods, the utility is limited to those recited methods and there is no well-established utility for such methods.

Claims 1 and 2 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Attorney Arguments Only (Alternative I)

Claims 1 and 2 have been rejected by the examiner under 35 U.S.C. § 101 and 35 U.S.C. § 112, ¶1. The examiner asserts that a credible utility has not been disclosed. Reconsideration under 37 CFR 1.111 is requested.

Anti-aging is indeed a credible utility. In USP 5157031 to Schwartz et al., compounds related to dehydroepiandrosterone (DHEA) are stated as having an anti-aging utility. Long-term treatment with DHEA itself is also known to delay the rate of aging. See column 1, lines 60-64 and column 2, lines 41-42. The patented compounds exhibit the same effects of DHEA, but are more potent and produce no estrogenic effects.

This is similar to the fact pattern in In re Brana, 34 USPQ 2d 1436 (Fed. Cir. 1995). In Brana the court reversed the examiner's rejection under 35 U.S.C. § 112, ¶ 1 because the antitumor compounds at issue therein were disclosed by the applicant as superior to known antitumor agents. This *inter alia* was deemed sufficient to render credible the disclosed anti-cancer utility. See footnote 9 in Brana wherein the court notes the examiner's statement that a rejection under 35 U.S.C. § 101 for failure to disclose a practical utility also could have been made.

The examiner is also reminded that a patent is presumed valid under 35 U.S.C. 282. The examiner in the Schwartz et al. patent could have required cancellation of any utility which he deemed incredible (In re Gottlieb, 140 USPQ 665 (CCPA 1964) and Ex parte Hozumi, 3 USPQ 2d 1059 (Bd. Pat. App and Inter. 1984)), but he did not. Accordingly, one may presume that the utility disclosed in Schwartz et al. is a valid, credible utility.

Examiner's Response to Attorney Arguments Only (Alternative I)

Claims 1 and 2 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a credible asserted utility or a well-established utility for the reasons of record.

Claims 1 and 2 are rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Applicants' arguments have been considered, but are not deemed persuasive.

Schwartz et al. disclose anti-aging as one among many utilities, including treatment and/or prevention of cancer, obesity, diabetes, and hyperlipidemia. The claims of Schwartz et al. are process claims limited to prophylaxis of obesity only. No actual anti-aging data are disclosed in Schwartz et al. Thus this fact pattern is not analogous to the fact pattern of Brana. In In re Brana

the issue was anti-leukemic activity of compounds based on evidence obtained in art recognized models validated with analogous compounds.

Failure of the examiner in Schwartz et al. to require cancellation of the anti-aging utility does not prove that said utility is credible. Examiners do not require applicant to delete reference to utilities which are not recited in the claims and which are not specific, substantial and credible. See e.g., "Discussion of Public Comments," Final Utility Examination Guidelines, 60 FR 36263 (1995) 1177 O.G. 146 (1995).

Attorney Arguments Only (Alternative II)

Claims 1 and 2 have been rejected by the examiner under 35 U.S.C. § 101 and 35 U.S.C. § 112, ¶1. The examiner asserts that a credible utility has not been disclosed. Reconsideration under 37 CFR 1.111 is requested.

Applicants submit that even if, *arguendo*, anti-aging is not a credible utility, applicants have nevertheless satisfied the utility requirement because another utility is disclosed in the specification as filed. Example IV discloses the instant compound A when formulated for topical administration is effective in retarding the wrinkling of skin. Since only one utility is necessary to satisfy 35 U.S.C. § 101, applicants submit that the examiner's rejection is in error and should be withdrawn.

Examiner's Response to Attorney Arguments Only (Alternative II)

Claims 1 and 2 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a credible asserted utility or a well-established utility for the reasons of record.

Claims 1 and 2 are rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Applicants' arguments have been considered, but are not deemed persuasive. Applicants are not claiming compound A. If compound A was being claimed, then any disclosed utility could be attributed thereto. However, since method of use claims are involved herein, applicants are limited to the utility set forth in those claims, i.e. retarding or preventing the entire process of aging. Claims amended so as to be drawn to a method of retarding wrinkling of skin by topical administration of compound A would obviate this rejection.

Attorney Arguments with Evidence (Alternative III)

Claims 1 and 2 have been rejected by the examiner under 35 U.S.C. § 101 and 35 U.S.C. § 112, ¶1. The examiner asserts that a credible utility has not been disclosed. Reconsideration under 37 CFR 1.111 is requested.

In support of applicants' statement of utility, attached hereto is a declaration under 37 CFR 1.132 by the inventors which shows unequivocally that the claimed compound A markedly reduces wrinkling of the skin when applied topically to the human face. The effect is long-lasting as shown in the data in Table 1.

Applicants submit that the claims encompass topical administration. Note page 20 of the specification which sets forth the various modes of administration, including topical administration. Applicants' data in the Rule 132 declaration evince a true retardation of skin wrinkling, evidence that the aging process is indeed retarded. It is not an incredible leap from retardation to prevention. One need only begin applying the material before the onset of wrinkling to lead to prevention.

Examiner's Rebuttal to Attorney Arguments with Evidence (Alternative III)

Claims 1 and 2 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a credible asserted utility or a well-established utility for the reasons of record.

Claims 1 and 2 are rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Applicants' arguments and declaration under 37 CFR 1.132 have been considered, but are not deemed persuasive.

The claims recite retardation or prevention of aging and are given their broadest reasonable interpretation when read in light of and consistent with the specification. It is evident that retardation and/or prevention of the **entire** aging process is intended. As noted in the first Office action, skin wrinkling is but a single external manifestation of the general process of aging. One cannot conclude from applicants' data that internal organs have ceased aging because wrinkling on a test subject's face has been reduced by cosmetic application of compound A. Physiological aging is a multifaceted process which does not involve a single chemical or biological effect. This is evident in the various theories that exist, such as loss of telomerase activity and the relationship of the telomere length to cell death as well as accumulation of DNA mutations and temporal genes that regulate the output of structural genes.

Claims amended so as to be drawn to a method of retarding wrinkling of skin by topical administration of compound A would obviate this rejection.

Example 3: Therapeutic Proteins

Specification: The specification discloses a protein having the amino acid sequence of SEQ ID NO: 1 and discloses that the protein can be made by protein synthesis techniques well known in the art. The only disclosed utility for the protein is for curing Alzheimer's disease. There is no other disclosure of any chemical, physical, or biological properties of the protein. There are 98 pages of specification which disclose alternate administration techniques and dosages that are very specific, conventional techniques for protein administration. There are no working examples that demonstrate the specifically asserted utility.

Claim: 1. The isolated protein consisting of the amino acid sequence set forth in SEQ ID NO: 1.

Analysis: The following analysis includes the questions that need to be asked according to the guidelines and the answers to those questions based on the above facts:

1) Based on the record, is there a "well established utility" for the claimed invention? The specification as filed does not disclose or provide any evidence that points to an activity for the protein and furthermore there is no art of record that discloses or suggests any activity for the claimed protein. Therefore there is no well-established utility.

2) Has the applicant made any assertion of utility for the specifically claimed invention? Here, there is an asserted utility, i.e., curing Alzheimer's disease.

3) Is the asserted utility specific? Curing Alzheimer's disease, a well known disease, clearly defines a use that depends upon the particular protein disclosed. Therefore, the utility is specific.

4) Is the asserted utility "substantial"? Since a cure for Alzheimer's disease is a desirable outcome based upon a need in the art, the disclosed use of the claimed protein is substantial and "real world".

5) Is the asserted "specific and substantial utility" credible? To answer this question one must keep in mind what one skilled in the art already knows. With respect to Alzheimer's disease, one skilled in the art knows that the disease has no known cure, no known cause or mechanism, and can not even be definitively assigned as a differential diagnosis in the absence of a post mortem examination. While the specification discloses conventional protein administration techniques, it does not include any working examples. It would be reasonable to conclude that the utility would not be credible based on the evidence of record.

Thus, the conclusion that can be reached from this analysis is that both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should be made.

Assume for the moment that a first Office action on the merits was mailed to applicant which included utility rejections under 35 U.S.C. § 101 and § 112, first paragraph, for the reasons stated above. In response, applicant argues that while the specifically disclosed utility may not be credible, the claim is to a protein and that proteins, in view of their unique chemical structure, would have a "well established utility" as being a source of amino acids used for manufacturing supplements for vitamins or food, as protein supplements for animal food, or as an animal poison if the protein is toxic. Furthermore, it would not require undue experimentation to use the protein in any one of these manners. Thus, applicant argues, the utility rejections under 35 U.S.C. § 101 and § 112, first paragraph, are not appropriate. Such an argument should not be persuasive. A well established utility is a specific, substantial and credible utility which is well known, immediately apparent or implied by the specifications' disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. "Well established utility" is does not mean any utility that one can dream up for an invention or a nonspecific utility that would obviously apply to virtually every member of a very general class of materials, such as proteins or DNA. If this were the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as landfill or a paper weight, any carbon containing molecule would have a "well established utility" as a fuel since it can be burned, and any protein would have the above noted well established utilities. This is not the intention of the statute.

Example 4: Uncharacterized Proteins

Specification: The specification discloses a protein having the amino acid sequence of SEQ ID NO: 1 and discloses that the protein can be made by protein synthesis techniques well known in the art. There is no disclosed utility and no description of the chemical, physical, or biological properties for the protein other than the sequence.

Claim: 1. The isolated protein consisting of the amino acid sequence set forth in SEQ ID NO: 1.

Analysis: The following analysis includes the questions that need to be asked according to the guidelines and the answers to those questions based on the above facts:

1) Based on the record, is there a "well established utility" for the claimed invention? The specification as filed does not disclose or provide any evidence that points to an activity for the protein. Additionally, there is no art of record that discloses or suggests any activity for the claimed protein. Therefore there is no well-established utility.

2) Has the applicant made any assertion of utility for the invention? No.

Thus, the conclusion of this analysis is that both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should be made.

Examiner's Rejection

Claim 1 is rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well- established utility.

The claimed protein is not supported by either a specific and substantial asserted utility or a well established utility because the specification fails to assert any utility for the protein and neither the specification as filed nor any art of record disclose or suggest any activity for the protein such that any utility would be well established for the protein.

Claim 1 is also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Attorney Arguments

Claim 1 has been rejected by the examiner under 35 U.S.C. § 101 and 35 U.S.C. § 112, ¶1. The examiner's position is that there is neither an asserted utility nor a well-established utility for the claimed protein. Reconsideration under 37 CFR 1.111 is requested.

While the specification may not specifically assert a utility for the claimed protein, proteins as a general class of compounds have a well-established utility in view of their unique chemical structure. Specifically, because of the unique chemical structure of the claimed protein, it has a well

established utility as being a source of amino acids used for manufacturing supplements for vitamins or food, as protein supplements for animal food, or as an animal poison if the protein is toxic. Furthermore, it would not require undue experimentation to use the protein in any one of these manners. Thus, the utility rejections under 35 U.S.C. § 101 and § 112, first paragraph, are not appropriate and should be withdrawn.

Examiner's Response to Attorney Arguments Only

Claim 1 is rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility because of the reasons set forth in the previous Office action.

Claim 1 is also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

Applicant's arguments have been fully considered but they are not deemed persuasive. Applicant argues that the claimed protein has a well established utility as being a source of amino acids used for manufacturing supplements for vitamins or food, as protein supplements for animal food, or as an animal poison if the protein is toxic. This is not persuasive. A "well-established utility" is a specific, substantial and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled

in the art. Neither a "well-established utility" nor a "specific utility" applies to any utility that one can dream up for an invention or even a utility that would apply to virtually every member of a general class of materials, such as proteins or DNA. If this were the case, any product or apparatus, including a perpetual motion machine, would have a well-established utility as landfill or a paper weight; any carbon containing molecule would have a well established utility as a fuel since it can be burned; and any protein would have the above noted "well established" or "specific" utilities. This is not the intention of the statute.

Example 5: Partially Characterized Proteins

Specification: The specification discloses a protein having the amino acid sequence of SEQ ID NO: 1 and discloses that the protein can be made by protein synthesis techniques well known in the art. There is no explicitly disclosed utility for the protein. However, there is an example which demonstrates that when the protein is contacted with whole blood, the protein will specifically bind with another protein X such that X can be isolated and quantified.

Claim: 1. The isolated protein consisting of the amino acid sequence set forth in SEQ ID NO: 1.

Analysis: The following analysis includes the questions that need to be asked according to the guidelines and the answers to those questions based on the above facts:

1) Based on the record, is there a "well established utility" for the claimed invention? Here, the specification as filed does disclose or provide evidence that points to an activity for the protein, i.e., when contacted with whole blood, it will specifically bind to protein X to enable the isolation and quantification of X. Assuming that the art does not disclose anything regarding the significance of X, or the examiner is unaware of any such art, then it would be reasonable to conclude that there is no "well established utility".

2) Has the applicant made any assertion of utility for the invention? Yes. The presence of an example may be an implicit assertion. In this case there is an implicit assertion that the claimed protein binds protein X.

3) Is the asserted utility specific? Yes. In this case the example indicates that when the protein is contacted with whole blood, the claimed protein will specifically bind to protein X.

4) Is the asserted utility substantial? No. There is no disclosed or real world utility associated with the claimed protein. Further experimentation is necessary to attribute a utility to the claimed protein. *See Brenner v. Manson*, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

Thus, the conclusion of this analysis is that both a 35 U.S.C. §101 rejection and a 35 U.S.C. §112 first paragraph rejection should be made.

Note: If the art disclosed at the time of filing that, e.g., an increased level of X correlates with an increased risk of heart disease, the claimed invention may have a well-established utility.

Example 6: Therapeutic Antibodies

Specification: The specification discloses a pharmaceutical composition containing a carrier, a non-antibody protein X and an antibody, said composition being suitable for treating HIV-1 infections. The specification further discloses a method of treating a subject by administering to the subject an amount of the above noted pharmaceutical composition effective to reduce the likelihood of the subject's becoming infected with HIV-1. The specification also discloses a vaccine for HIV-1 comprising the non-antibody protein X.

The specification further discloses a method of treating an HIV-infected subject, which includes administering to the subject an amount of the composition of the invention effective to reduce the rate of spread of HIV-1 infection in the subject.

The specification also discloses a method of decontaminating a fluid containing HIV-1 which comprises contacting the fluid with the composition of the invention under conditions such that the composition of the invention forms a complex with the HIV-1 therein and removing the complex so formed from the fluid, thereby decontaminating the fluid.

Claims: The following claims are pending in the application:

1. A composition comprising (a) a pharmaceutically acceptable carrier, (b) a non-antibody protein X, and (c) an antibody, said composition being suitable for treating HIV-1 infections.

2. A method of treating an HIV-1 infected subject, which comprises administering to the subject an amount of the composition of claim 1 effective to reduce the rate of spread of HIV-1 infection in the subject.

3. A method of decontaminating a fluid containing HIV-1, which comprises contacting the fluid with the composition of claim 1 under conditions such that the composition of claim 1 forms a complex with the HIV-1 therein and removing said complex from the fluid, thereby decontaminating the fluid.

4. A method of preventing a subject from becoming infected with HIV-1 comprising administering to the subject an amount of the composition of claim 1 effective to prevent the subject from becoming infected with HIV-1.

5. A method of preventing or treating HIV-1 infection which comprises administering to a subject the composition of claim 1.

6. A vaccine for HIV-1 comprising a non-antibody protein X.

Analysis: The following analysis includes the questions that need to be asked according to the guidelines and the answers to those questions based on the above facts:

1) Based on the record, is there a "well established utility" for the claimed invention? The specification as filed does not disclose or provide

any evidence that points to an activity for the compositions (claims 1 and 6) such that another non-asserted utility would be well established. Additionally, there is no art of record that discloses or suggests any activity for the claimed compositions such that another non-asserted utility would be well established. With respect to the method claims (claims 2-5), since each of these claims is directed to a specific method of use, the utility of each claim is limited to that use and the examiner should not look to a "well established utility" for the composition used in each claimed method. Consequently, the answer to the question is no for all of the claims.

2) Has the applicant made any assertion of utility for the specifically claimed invention? For each of the claims presented for this example, an asserted utility can be found. Those utilities are (1) a composition for treating HIV-1 infections (claim 1); (2) a vaccine against HIV-1 (claim 6); (3) a method of treating a subject infected with HIV-1 (claim 2); (4) a method of decontaminating a fluid containing HIV-1 (claim 3); and (5) a method of preventing a subject from becoming infected with HIV-1 (claims 4 and 5).

3) Is the asserted utility specific? HIV-1 infection is a known problem and the utilities noted in 2) above are disclosed uses that depend upon the particular protein disclosed. Therefore, the utility is specific.

4) Is the asserted utility substantial? Since all of the asserted utilities are practical based upon a need in the art, the disclosed utilities are substantial and "real world".

5) Is the asserted "specific and substantial utility" credible? The answer to that question for claims 1-3, 5 (treating part) and 6 is yes in that all of these claims are directed to subject matter which one would believe is credible. Those credible utilities are listed above in 2). However, claim 4 and part of claim 5 are directed to a method of preventing a subject from becoming infected with HIV-1. The term infection, given its broadest reasonable interpretation consistent with the specification, merely requires that one such virus gain entry into the cells of a host. Given that there are no compounds known that would be capable of preventing entry into every cell with 100% efficiency then the utility for this claim would not be credible.

Thus, the conclusion that can be reached from this analysis is that no rejection under 35 U.S.C. § 101 should be made against claims 1-3 and 6 but that both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should be made against claim 4. For claim 5, since only one utility is needed for the claim to meet the criterion for 35 U.S.C. § 101 and the treatment of HIV-1 infection meets this criterion, no rejection for lack of utility should be made against claim 5. The presence of the utility that is not credible in claim 5 (preventing HIV-1 infection) should be addressed under 35 U.S.C. § 112, first paragraph, scope of enablement.

Example 7: Chemical therapeutics

Specification: The specification discloses compound A where A is a stable 8-10 membered bicyclic aromatic heterocyclic having 1-3 heteroatoms selected from the group consisting of P, Se and Si. These compounds are disclosed to be useful in the inhibition of HIV protease, the prevention or treatment of infection by the human immunodeficiency virus (HIV) and the treatment of consequent pathological conditions such as AIDS. Treating AIDS or preventing or treating infection by HIV is defined as including, but not limited to, treating a wide range of states of HIV infection: AIDS, ARC (AIDS related complex), both symptomatic and asymptomatic, and actual or potential exposure to HIV. For example, the compounds of this invention are useful in treating infection by HIV after suspected past exposure to HIV by, e.g., blood transfusion, organ transplant, exchange of body fluids, bites, accidental needle stick, or exposure to patient blood during surgery.

An assay for inhibition of microbial expressed HIV protease and a cell spread assay are disclosed. Compound X, a species of the generic invention is tested in these assays.

Claims:

1. A compound of the formula:

A

where A is a stable 8-10 membered bicyclic aromatic heterocyclic having 1-3 heteroatoms selected from the group consisting of P, Se and Si.

2. A composition comprising a compound of claim 1, for use in the treatment of AIDS, in the prevention of infection by HIV, in the treatment of infection of HIV, or in the inhibition of HIV protease, and a carrier.

3. A method of treating AIDS, comprising administering to a mammal in need of such treatment an effective amount of a compound of claim 1.

4. A method of preventing infection by HIV, comprising administering to a mammal in need of such treatment an effective amount of a compound of claim 1.

5. A method of treating infection by HIV, comprising administering to a mammal in need of such treatment an effective amount of a compound of claim 1.

6. A method of inhibiting HIV protease, comprising administering to a mammal in need of such treatment an effective amount of a compound of claim 1.

7. A method of delaying the onset of AIDS, comprising administering to a mammal in need of such treatment an effective amount of a compound of claim 1.

Analysis: The following analysis includes the questions that need to be asked according to the guidelines and the answers to those questions based on the above facts:

1) Based on the record, is there a "well established utility" for the claimed invention? The specification as filed does not disclose or provide any evidence that points to an activity for the compound and composition (claims 1-2) such that another non-asserted utility would be well established. Additionally, there is no art of record that discloses or suggests any activity for the claimed compound and composition such that another non-asserted utility would be well established. Therefore the answer is no for claims 1 and 2. With respect to the method claims (claims 3-7), since each of these claims is directed to a specific method of use, the utility of each claim is limited to that use and the examiner should not look to a "well established utility" for the composition used in each claimed method.

2) Has the applicant made any assertion of utility for the specifically claimed invention? Looking at each of the claims presented for this example, you will find an asserted utility for each of them. Those utilities are (1) methods of treating AIDS or subjects infected with HIV (claims 3

and 5); (2) a method of preventing infection by HIV (claim 4); (3) a method of inhibiting HIV protease (claim 6); (4) a method for delaying the onset of AIDS (claim 7). The compound of claim 1 and the composition of claim 2 are disclosed to be useful in any of the above utilities.

3) Is the asserted utility specific? Since the claims are drawn to compound A (a relatively small genus) and various methods of using A, and because the claimed processes require the use of A, the utilities are specific.

4) Is the asserted utility substantial? Since HIV infection is a known problem, the utilities noted in 2) above clearly define a "real world" context of use and therefore are substantial utilities.

5) Is the asserted "specific and substantial utility" credible? The answer to that question for claims 1-2 (utilities other than preventing infection by HIV), 3, and 5-7 is yes in that all of these claims are directed to subject matter which one of skill in the art would believe is credible. Those credible utilities are listed above in 2). However, claim 4 is directed to a method of preventing a subject from becoming infected with HIV. The term infection, given its broadest reasonable interpretation consistent with the specification, merely requires that one such virus gain entry into the cells of a host. Given that there are no compounds known that would be capable of preventing entry into every cell with 100% efficiency then the utility for this claim would not be credible.

Thus, no rejection under 35 U.S.C. § 101 should be made against claims 3 and 5-7 but both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should be made against claim 4. For claim

1, since it is a product claim that does not recite any utilities, only one credible asserted utility is needed to meet the criteria for 35 U.S.C. § 101. Any of the asserted utilities, other than preventing HIV infection, meets this criteria and, accordingly, no rejection under 35 U.S.C. § 101 should be made against claim 1. For claim 2, since only one utility is needed for the claim to meet the criteria for 35 U.S.C. § 101 and the claimed utilities, other than preventing HIV infection, meet this criteria, no rejection under 35 U.S.C. § 101 should be made against claim 2. The presence of the utility that is not credible in claim 2 (preventing HIV infection) should be addressed under 35 U.S.C. § 112, first paragraph, scope of enablement.

Note that when examining the patentability of the composition of claim 2, the statement of intended use should be treated as a claim limitation when considering compliance with the requirement of 35 U.S.C. §112, first paragraph. Examination should address the issue of whether one skilled in the art could make and use the claimed invention without undue experimentation such that it would operate in the manner recited in the claim.

Example 8: "Therapeutics" Not Associated with a Disease

Specification: Compound A is disclosed to inhibit enzyme XYZ, a well-known enzyme which is a member of the family of tyrosine kinases, *in vitro*. The specification states that compound A can be used to treat diseases caused or exacerbated by increased activity of enzyme XYZ. No actual diseases are named.

Claims:

1. Compound A.

2. A method of treating a disease caused or exacerbated by increased activity of enzyme XYZ consisting of administering an effective amount of compound A to a patient.

Analysis: The following analysis includes the questions that need to be asked according to the guidelines and the answers to those questions based on the above facts:

1) Based on the record, is there a "well established utility" for the claimed invention? With respect to claim 2, since the claim is directed to a specific method of use, the utility of this claim is limited to that use and the examiner should not look to a "well established utility" for the composition used in the claimed method. Consequently, the answer to the question is no for claim 2. With respect to claim 1, the answer is different. Enzymes catalyze certain reactions involving the enzyme substrate. Here, since enzyme XYZ is a well-known tyrosine kinase, the substrate for the enzyme and the reaction which the enzyme catalyzes must also be well known.

Since all of this is well known it is reasonable to infer that an inhibitor of enzyme XYZ, such as compound A, would have a "well-established utility" in controlling the enzyme/substrate interaction in the known reaction. Therefore, compound A has a "well established utility", no rejection under 35 U.S.C. § 101 should be made against claim 1, and there is no need to go further in the analysis with respect to claim 1.

2) Has the applicant made any assertion of utility for the specifically claimed invention? The answer is yes. Claim 2 has the asserted utility of treating a disease caused or exacerbated by increased activity of enzyme XYZ.

3) Is the asserted utility specific? In this case, the specification teaches that the claimed compound inhibits a particular enzyme (XYZ). Therefore, compound A has properties and uses that are not applicable to a general class of compounds. Therefore, the answer is that the invention of claim 2 has a specific utility.

4) Is the asserted utility substantial? Since neither the specification nor the art of record disclose any diseases or conditions caused or exacerbated by enzyme XYZ, the asserted utility in this case essentially is a method of treating an unspecified, undisclosed disease or condition, which does not define a "real world" context of use. Treating an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Therefore, the answer to this question is no with respect to claim 2.

Therefore no rejection under 35 U.S.C. § 101 should be made against claim 1 but both a 35 U.S.C. § 101, as well as 35 U.S.C. § 112, first paragraph, utility rejection should be made against claim 2.

Once the rejection has been made with respect to claim 2, the applicant bears the burden of rebutting it. Upon receiving applicant's response, the examiner should review the original disclosure, any evidence relied upon in establishing the utility rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, any amendments and any new reasoning or evidence provided by the applicant in support of the asserted utility.

The following situations are most probable:

(1) Applicant provides a reference, published before the filing date of the application, which teaches that certain diseases are associated with increased activity of enzyme XYZ. In this case the examiner should withdraw the utility rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, for claim 2.

(2) Applicant submits an opinion declaration under 37 C.F.R. 1.132 by a qualified person of skill in the art which states that specific disease conditions are known to the skilled artisan to be either caused or exacerbated by increased activity of enzyme XYZ. The declarant identifies specific diseases and/or conditions. After reviewing the record in its entirety, the Examiner should only maintain this rejection if evidence of more probative value than the declaration exists which establishes a basis for doubting the objective truth of the declaration. Unsupported scientific reasoning is not more probative than the declaration. If the examiner maintains the rejection,

the examiner must provide documentation on the record which establishes the basis of doubting the statements made in the declaration.

(3) Applicant submits a declaration under 37 C.F.R. 1.132 which contains a factual showing that compound A is effective in alleviating the symptoms of peptic ulcers. The declaration also contains a factual showing that peptic ulcers are exacerbated by increased activity of enzyme XYZ. The facts are adequate to show that as of the date for which priority was sought, compound A was known to be effective in alleviating the symptoms of peptic ulcers. The rejection under 35 U.S.C. 101 and 112 would be withdrawn.

Example 9: DNA Fragments

Specification: The specification discloses 4332 nucleic acid sequences that were obtained from a human cDNA library that was formed using human epithelial cells. The sequences, SEQ ID NOS: 1-4332, are believed by applicant to be fragments of full length genes. Thus, the specification discloses that all of the sequences comprise at least part of the coding sequence for a protein that is actually produced in the human cells. The specification discloses how to use each of the 4332 nucleic acid sequences as a probe to obtain the full length genes that correspond to the nucleic acid sequences, which full length genes can be used to recombinantly make the corresponding proteins, which can then be used to study the cellular mechanisms and activities in which the proteins are involved. There is a generic disclosure of how to recombinantly make the corresponding protein from each of the sequences. The sequences vary in length. Some of the sequences are long enough to encode functional proteins, i.e., these sequences could be open reading frames.

No use is disclosed for any of the putative proteins other than the possibility of using them to identify and study the cellular mechanisms and activities in which the proteins are involved.

Claim 1. A cDNA consisting of the sequence set forth in SEQ ID NO: 1.

Analysis: The following analysis includes the questions that need to be asked according to the guidelines and the answers to those questions based on the above facts:

1) Based on the record, is there a "well established utility" for the claimed invention? The specification as filed does not disclose or provide any evidence that points to an activity for the cDNA or the proteins that can be obtained using the cDNA such that another non-asserted utility would be well established. Additionally, there is no art of record that discloses or provides any evidence that points to an activity for the target cDNA or the proteins that might be obtained using the target cDNA to be obtained such that another non-asserted utility would be well established. Consequently, the answer to the question is no.

2) Has the applicant made any assertion of utility for the specifically claimed invention? Here, there is an asserted utility, i.e., each cDNA can be used as a probe to obtain the full length gene that corresponds to the cDNA molecule, which full length gene can be used to recombinantly make the corresponding protein, which can then be used to study the cellular mechanisms and activities in which the protein is involved.

3) Is the asserted utility specific? The answer to this question is no. The use of the claimed nucleic acid is not particular to the sequence being claimed because it would be applicable to the general class of cDNAs. Any partial nucleic acid prepared from any cDNA may be used to as a probe in the preparation and or identification of a full-length cDNA.

4) Is the asserted utility substantial? The answer to this question is no. As seen in 2) above, the asserted utility for the claimed cDNA is a method of making the corresponding protein. Thus, to determine whether or not this method has a "substantial utility," it must be determined whether or not the corresponding protein, has a "substantial utility." Here, the only utility

asserted for the protein is for identifying and studying the properties of the protein itself or the mechanisms in which the protein is involved. This does not define a "real world" context of use. Since the asserted utility for the protein (identifying and studying the properties of the protein itself or the mechanisms in which the protein is involved) does not define a "real world" context of use, a method of making that protein also could not define a "real world" context of use. In fact, both utilities would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use.

Thus, the conclusion reached from this analysis is that both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should be made.

Examiner's Rejection

Claim 1 is rejected under 35 U.S.C. § 101 because the claimed invention is not supported by specific and substantial utility or a well-established utility.

The claimed cDNA compound is not supported by a specific asserted utility because the disclosed use of the nucleic acid is generally applicable to any nucleic acid and therefore is not particular the nucleic acid sequence being claimed. Further, the claimed cDNA compound is not supported by a substantial utility because the specification states only that the cDNA compounds are useful as probes for assisting in the isolation of full-length cDNAs or genes which would be used to make protein. Once the protein is obtained, the protein would be used in conducting research to functionally

characterize the protein. A starting material that can only be used to produce a final product does not have a substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case none of the proteins that are to be produced as final products resulting from processes involving the claimed cDNA have asserted or identified specific and substantial utilities. The research contemplated by Applicants to characterize potential protein products, especially their biological activities, does not constitute a specific and substantial utility. Identifying and studying the properties of the protein itself or the mechanisms in which the protein is involved does not define a "real world" context of use. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the cDNA compounds such that another non-asserted utility would be well established for the compounds.

Claim 1 is also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

Example 10: <u>DNA Fragment encoding a Full Open Reading Frame (ORF)</u>

Specification: The specification discloses that a cDNA library was prepared from human kidney epithelial cells and 5000 members of this library were

sequenced and open reading frames were identified. The specification discloses a Table that indicates that one member of the library having SEQ ID NO: 2 has a high level of homology to a DNA ligase. The specification teaches that this complete ORF (SEQ ID NO: 2) encodes SEQ ID NO: 3. An alignment of SEQ ID NO: 3 with known amino acid sequences of DNA ligases indicates that there is a high level of sequence conservation between the various known ligases. The overall level of sequence similarity between SEQ ID NO: 3 and the consensus sequence of the known DNA ligases that are presented in the specification reveals a similarity score of 95%. A search of the prior art confirms that SEQ ID NO: 2 has high homology to DNA Ligase encoding nucleic acids and that the next highest level of homology is to alpha-actin. However, the latter homology is only 50%. Based on the sequence homologies, the specification asserts that SEQ ID NO: 2 encodes a DNA ligase.

Claim 1: An isolated and purified nucleic acid comprising SEQ ID NO: 2.

Analysis: The following analysis includes the questions that need to be asked according to the guidelines and the answers to those questions based on the above facts:

1) Based on the record, is there a "well established utility" for the claimed invention? Based upon applicant's disclosure and the results of the PTO search, there is no reason to doubt the assertion that SEQ ID NO: 2 encodes a DNA ligase. Further, DNA ligases have a well-established use in the molecular biology art based on this class of protein's ability to ligate DNA. Consequently the answer to the question is yes.

Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed. In order to determine whether the claimed invention has a well-established utility the examiner must determine that the invention has a specific, substantial and credible utility that would have been readily apparent to one of skill in the art. In this case SEQ ID NO: 2 was shown to encode a DNA ligase that the artisan would have recognized as having a specific, substantial and credible utility based on its enzymatic activity.

Thus, the conclusion reached from this analysis is that a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should not be made.

Example 11: <u>Animals with Uncharacterized Human Genes</u>

Specification: Kidney cells from a patient with Polycystic Kidney (PCK) Disease have been used to make a cDNA library. From this library 8000 nucleotide "fragments" have been sequenced but not yet used to express proteins in a transformed host cell nor have they been characterized in any other way. The 50 longest fragments, SEQ ID NO: 1-50, respectively, have been used to make transgenic mice. None of the 50 lines of mice have developed Polycystic Kidney Disease to date. The asserted utility is the use of the mice to research human genes from diseased human kidneys. The disease is inheritable, but chromosomal loci have not yet been identified. Neither the absence or presence of a specific protein has been identified with the disease condition.

Claims: 1. A non-human animal in which all of the somatic and germ cells contain DNA having SEQ ID NO: 1.

2. A non-human animal in which all of the somatic and germ cells contain DNA having SEQ ID NO: 2.

[3. - 50. are identical in form to 1 and 2 with the sequence number corresponding with the claim number in each.]

51. A method of screening for potential causative agents which trigger or exacerbate Polycystic Kidney Disease comprising administering a selected agent to a non-human animal of any one of claims 1 -50 and observing the kidney of said animal for abundant cyst formation.

Analysis: The following analysis includes the questions that need to be asked according to the guidelines and the answers to those questions based on the above facts:

1) Based on the record, is there a "well established utility" for the claimed invention? The specification as filed does not disclose or provide any evidence that points to a property of the claimed animals (claims 1-50) such that another non-asserted specific and substantial credible utility would be well established. Additionally, there is no art of record that discloses or provides any evidence that points to a property of the claimed animals (claims 1-50) such that another non-asserted specific and substantial credible utility would be well established. With respect to claim 51, since it is directed to a specific method of use, the utility of this claim is limited to that use and the examiner should not look to a "well established utility" for the

composition used in the claimed method. Consequently, the answer to the question is no.

2) Has the applicant made any assertion of utility for the specifically claimed invention? Here, there is an asserted utility, i.e., to use the animals to research human genes from diseased human kidneys, specifically to use the animals in a method for screening for potential causative agents which trigger or exacerbate Polycystic Kidney Disease.

3) Is the asserted utility specific? The answer to this question is yes. In this case, the sequences (claims 1-50 and the full length counterparts of the other 7950 nucleic acid fragments) are asserted to be useful to generate the non-human animals as instantly claimed, and to use the animals in a screening method for PCK.

4) Is the asserted utility substantial? The answer to this question is yes because a disease model for PCK disease is a real world context of use.

5) Is the asserted utility credible? The answer to this question is no. In this case it is noted in the specification that none of the 50 lines of mice that have been transformed with the claimed DNAs have developed Polycystic Kidney Disease to date. Additionally, there is no indication that the absence or presence of a specific protein is associated with the disease condition.

Thus, the conclusion that can be reached from this analysis is that both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, rejection should be made.

Examiner's Rejection

Claims 1-51 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a credible asserted utility or a well-established utility.

Neither the specification as filed nor any art of record discloses or suggests any specific property or activity for the animals such that a utility would be well established for the animals.

Further, the claimed animals and method of screening are not supported by a credible utility because the specification states that none of the transgenic animals exhibited PCK disease. The asserted use of the animals is for research in human genes from diseased kidneys however the specification indicates that they were unable to get an operative model. Since there is no evidence on the record that there are operative transgenic animal models for this research, the asserted utility is inoperative and is therefore not credible.

With regard to the asserted use of the animals as disease models, the action of the human DNA compounds on the animals is not specifically known and the mere assertion that abundant cyst formation will be observable in any of the claimed animals would not be accepted by one skilled in the art as being reasonable or credible in view of the contemporary knowledge in the art. As discussed by A. Cure et al. (a 1995 reference), while extensive studies have been conducted, the only clear results are from Mendelian studies of families that exhibit the disease. These studies indicate that the disease is inheritable and dominant, as opposed to recessive, via statistical analysis. No study has clearly indicated that a single DNA component is involved. No chromosomal loci have been identified. The

possibility of a regulatory mechanism being involved has not been ruled out by any of the studies conducted to date. No specific protein or abnormal level of a specific protein has been associated with the disease. The expectation that any of the claimed animals will exhibit the abundant cyst formation based on the presence of a single, unidentified DNA compound is not credible based on the specification's evidence to the contrary.

Claims 1-51 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Attorney Arguments Only (Alternative I)

Claims 1-51 have been rejected by the examiner under 35 U.S.C. § 101 and 35 U.S.C. § 112, ¶1. The examiner asserts that a substantial utility has not been disclosed. Reconsideration under 37 CFR 1.111 is requested.

The use of these animals to study DNA and polycystic kidney disease via observing abundant cyst formation is credible. This utility is directly analogous to that of US Patent No. 4,736,866 to Leder et al. in which human DNA compounds associated with tumor formation are contained in the genomes of non-human animals and these animals are used to study the human DNA compounds and tumor formation as well as tumor treatment. Such an important medical research utility as exists for the current claimed invention is a patentable utility. The claimed animals contain DNA

compounds that are associated with human cells which exhibit the specific disease, just as they were in the Leder et al. patent.

Examiner's Response to Attorney Arguments Only (Alternative I)

Claims 1-51 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a credible asserted utility, or a well established utility for the reasons of record.

Claims 1-51 are rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility, or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the invention so that it would operate as intended without undue experimentation.

Applicants' arguments have been considered, but are not deemed persuasive. Applicants analogize the current specification, animals and intended utilities to those of Leder et al. US Patent No. 4,736,866. The situations are in fact not analogous. The specific embodiment of the specific MYC oncogene in the Leder et al. patent involved a well-established oncogene. There was no question in the art that the particular DNA compound had been directly associated with tumor formation in humans. Moreover, the specific mice disclosed in the Leder et al. specification exhibit tumor formation. It does not directly follow that a diseased cell will necessarily contain "culprit" DNA as asserted by Applicants. This is particularly true of cDNA compounds as used herein, where no protein effect is associated with the disease, nor are there any operative animal models that exhibit this disease state and the evidence of record is contrary

to the desired result. Thus, even if one were to accept the premise that the diseased cell must contain a genetic flaw, no transgenic model is disclosed in currently available form.

Attorney Arguments with Evidence (Alternative II)

Claims 1-51 have been rejected by the examiner under 35 U.S.C. § 101 and 35 U.S.C. § 112, ¶1. The examiner asserts that a credible utility has not been disclosed. Reconsideration under 37 CFR 1.111 is requested.

In support of applicant's statement of utility, attached hereto is a declaration submitted under 37 CFR 1.132 by the inventors which describes a mouse corresponding to the animal of claim 38 which has exhibited abundant cyst formation. This effect has been confirmed as evidenced in the declaration, by the production of three additional founder mice that carry DNA SEQ ID NO: 38 as a transgene and have exhibited abundant cyst formation. In addition, as evidenced in the declaration, these mice have been cross-bred and some of their progeny exhibit the abundant cyst formation as well.

Based on this evidence clearly the use of the claimed animals to screen for agents which trigger or exacerbate the disease condition is substantial and credible.

Examiner's Response to Attorney Arguments with Evidence (Alternative II)

The examiner should withdraw the rejection of claim 38 based on lack of credible utility in light of this evidence. However, the other product

claims should still be rejected under 35 U.S.C. §101 and 35 U.S.C. §112 first paragraph as lacking credible utility and claim 51 should still be rejected under 35 U.S.C. §112 first paragraph as lacking an enabling disclosure except as it depends on claim 38.

Example 12: Receptors

Specification: The specification discloses a protein, isolated from a cell membrane preparation, which is the binding partner for protein X. The specification does not characterize the isolated protein with regard to its biological function or any disease or body condition that is associated with the isolated protein. Based solely on the fact that the protein was isolated from a cell membrane and it binds to protein X, applicant characterizes the isolated protein as receptor A. The function of protein X has also not been identified. The specification discloses a binding assay for determining other materials which bind to the receptor by adding the material to the complex of receptor A and protein X and determining the amount of inhibition of the binding of the complex as an indication that the material will bind to the receptor and thus be a therapeutic drug to effect control over the receptor. Also disclosed is the production of a monoclonal antibody that specifically binds to receptor A. There are no working examples using any materials to demonstrate such inhibition of binding, to assay the receptor or to identify any other material which binds to the receptor. The utility disclosed is for identifying materials that bind the receptor and the potential use of such materials as therapeutics.

Claims:

1. Isolated receptor A.

2. A method of identifying materials which bind to receptor A comprising:

a) forming a complex of receptor A and protein X in a liquid;

b) adding a material to be screened to said complex;

c) determining the amount of binding of said complex wherein an inhibition of said binding is an indication that said material binds to said receptor.

3. A monoclonal antibody which specifically binds to receptor A.

Analysis: The following analysis includes the questions that need to be asked according to the guidelines and the answers to those questions based on the above facts. For this fact situation, each claim will be analyzed separately.

Claim 1:

1) Based on the record, is there a "well established utility" for the claimed invention? The specification as filed does not disclose or provide any evidence that points to a property of the claimed receptor such that another non-asserted utility would be well established. Additionally, there is no art of record that discloses or provides any evidence that points to a property of the claimed receptor such that another non-asserted utility would be well established. Consequently, the answer to the question is no.

2) Has the applicant made any assertion of utility for the specifically claimed invention? Here, there is an asserted utility for the claimed invention. In fact, for claim 1 there are two asserted utilities, i.e., a) a method of identifying materials which bind to receptor A, and b) a method of making a monoclonal antibody.

3) Is the asserted utility specific? The answer to this question is yes. In this case, the method of identifying materials which bind to a specific receptor, namely receptor A and a method of making monoclonal antibodies to receptor A are methods that are not applicable to the general class of receptors. Therefore, there is an asserted specific utility for the claimed invention.

4) Is the asserted utility substantial? The answer to this question in each case is no. The method in 2a) above is a method of identifying those materials which bind to receptor A. Thus, to determine whether or not this method has a "substantial utility," it must be determined whether or not the material that binds to receptor A itself has a "specific and substantial utility." Here, the only utility asserted for the identified materials is a therapeutic to effect control over receptor A. Since neither the specification nor the art of record disclose any diseases or conditions associated with receptor A, a method of treating an unspecified, undisclosed disease or condition, does not define a "real world" context of use. Further research to identify or reasonably confirm a "real world" context of use is required. Since the asserted utility for the identified materials does not define a "real world" context of use, a method of identifying such materials also could not define a "real world" context of use.

The method in 2b) above is a method of making a material, i.e., a monoclonal antibody. Thus, to determine whether or not this method has a "substantial utility", it must be determined whether or not the monoclonal antibody itself has a "specific and substantial utility." Here, there is an asserted utility for the monoclonal antibody even though it is not explicit,

e.g., as a therapeutic drug to effect control over the receptor. However, since neither the specification nor the art of record disclose any diseases or conditions associated with receptor A, the asserted utility in this case essentially is a method of treating an unspecified, undisclosed disease or condition, which does not define a "real world" context of use. Treating an unspecified, undisclosed disease or condition clearly would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. *See Brenner v. Manson*, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

Since the asserted utility for the product (monoclonal antibody) does not define a "real world" context of use, a method of making such a product also could not define a "real world" context of use.

Thus, the conclusion from analysis is that both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should be made on claim 1.

Claim 2:

1) Based on the record, is there a "well established utility" for the claimed invention? Since the claim is directed to a specific method of use, the utility of this claim is limited to that use and the examiner should not

look to a "well established utility" for the composition used in the claimed method. Consequently, there is no "well-established" utility for the method.

2) Has the applicant made any assertion of utility for the specifically claimed invention? Here, there is an asserted utility for the claimed invention, i.e., a method of identifying materials that bind to receptor A.

3) Is the asserted utility specific? The answer to this question is yes. In this case, the method of identifying materials which bind to a specific receptor, namely receptor A, is a method that is not applicable to the general class of receptors. It is specific to receptor A. Therefore, there is an asserted specific utility for the claimed invention.

4) Is the asserted utility substantial? The answer to this question is no. Specifically, the method essentially is a method of identifying a material, i.e., those materials which bind to receptor A. Thus, to determine whether or not this method has a "substantial utility", it must be determined whether or not the material that binds to receptor A itself has a "substantial utility." Here, the only utility asserted for the identified materials is a therapeutic to effect control over receptor A. Since neither the specification nor the art of record disclose any diseases or conditions associated with receptor A, the asserted utility in this case essentially is a method of treating an unspecified, undisclosed disease or condition, which does not define a "real world" context of use. Treating an unspecified, undisclosed disease or condition clearly would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. *See Brenner v. Manson*, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole

"utility" consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

Since the asserted utility for the identified materials does not define a "real world" context of use, a method of identifying such materials also could not define a "real world" context of use.

Thus, the conclusion is that both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should be made on claim 2.

Claim 3:

1) Based on the record, is there a "well established utility" for the claimed invention? The specification as filed does not disclose or provide any evidence that points to a property of the claimed monoclonal antibody such that another non-asserted utility would be well established. Additionally, there is no art of record that discloses or provides any evidence that points to a property of the claimed monoclonal antibody such that another non-asserted utility would be well established. Consequently, the answer to the question is no.

2) Has applicant made any assertion of utility for the specifically claimed invention? Here, there is no explicitly asserted utility for the claimed monoclonal antibody. However, as stated in the analysis of claim 1 above, there is an implied asserted utility for the monoclonal antibody even though it is not explicit, e.g., as a therapeutic drug to effect control over the receptor.

3) Is the asserted utility specific? The answer to this question is yes. In this case, the monoclonal antibody is specific for a specific protein, namely receptor A. Therefore, there is an asserted specific utility for the claimed invention.

4) Is the asserted utility substantial? The answer to this question is no. Specifically, since neither the specification nor the art of record disclose any diseases or conditions associated with receptor A, the asserted utility in this case is a method of treating an unspecified, undisclosed disease or condition, which does not define a "real world" context of use. Treating an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. *See Brenner v. Manson*, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

Thus, both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should be made on claim 3.

Caveat:

Let us assume for the moment that the specification also discloses that receptor A is present on the cell membranes of melanoma cells but not on the cell membranes of normal skin cells. Assume also that the examiner has found and made of record a journal article published prior to the

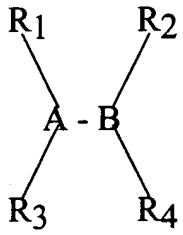
application's filing date indicating that it is desirable to selectively detect melanoma cells as opposed to normal skin cells so as to diagnose that type of cancer. Does this change the above analysis?

For each of the claims, the above analysis changes right from the first question: Based on the record, is there a "well established utility" for the claimed invention? The answer to this question would change to yes in each case. Specifically, based on this record, there is a "well established utility" for the products of claims 1 and 3. The "well established utility" for the receptor A is a method of assaying for materials that bind to receptor A by contacting the materials to a complex of receptor A and protein X. Furthermore, making a monoclonal antibody to receptor A for diagnosing melanoma would constitute a well-established utility. Such utilities are "well established" because the disclosure of the properties of the receptor and antibody taken together with the knowledge of one skilled in the art indicates that these specific, substantial and credible utilities were known. With respect to claim 2, since there is now evidence of record providing a correlation between this method and diagnosing melanoma, i.e., materials identified by the method, such as the monoclonal antibody, can be used to diagnose melanoma, this method now has a "well established utility".

Therefore, utility rejections under 35 U.S.C § 101 rejection and a 35 U.S.C. § 112, first paragraph, should not be made against claims 1-3.

Example 13: Large Chemical Groups

Specification: The specification discloses a genus of chemical compounds having the formula:

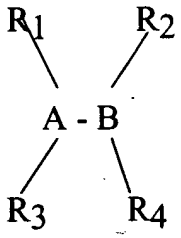


Wherein A, B and R1-R4 are defined.

The specification teaches the chemical synthesis methods necessary to make the compounds but does not disclose any chemically similar compounds. The specification provides several paragraphs describing basic experimental methods with known materials and suggests testing the claimed compounds in the same methods so as to ascertain the physical, chemical and biological properties of the claimed compounds. The only utility mentioned in the specification is that the compounds could be used for biomedical research once the physical, chemical and biological properties of the compounds have been determined.

Claims:

1. Compounds having the formula:



Analysis: The following analysis includes the questions that need to be asked according to the guidelines and the answers to those questions based on the above facts:

1) Based on the record, is there a "well established utility" for the claimed invention? The specification as filed does not disclose or provide any evidence that points to a property or activity of the claimed compounds such that another non-asserted utility would be well established. Additionally, the art of record does not disclose or provide any evidence that points to a property or activity of the claimed compounds such that another non-asserted utility would be well established. Consequently, the answer to the question is no.

2) Has the applicant made any assertion of utility for the specifically claimed invention? Here, there is an asserted utility, i.e., the claimed compounds can be used in biomedical research once the physical, chemical and biological properties of the compounds have been determined.

3) Is the asserted utility specific? The answer to this question is no. Any chemical compound can be used for biomedical research and experimental methods. This type of assertion is generic to the class of chemical compounds and therefore not specific to the claimed invention.

4) Is the asserted utility substantial? The answer to this question would be no. Biomedical research and even experimental methods for determining the physical, chemical, and biological properties of the compounds themselves do not define a "real world" context of use. Such utilities clearly would require or constitute carrying out further research to identify or reasonably confirm a "real world" context in which the compounds could be used. *See Brenner v. Manson*, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole utility consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

Thus, both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should be made.

Examiner's Rejection

Claim 1 is rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well- established utility. The claimed compounds are not supported by either a specific and substantial asserted utility or a well established utility because the specification states only that the compounds are useful for

biomedical research, and neither the specification as filed nor any art of record discloses or suggests any property or activity for the compounds such that another non-asserted utility would be well established for the compounds. The biomedical research contemplated by applicants is unspecified. It will take place at some future time, only when the properties of the claimed compounds might have been elucidated by the experimental methods disclosed in applicants' specification. Absent a disclosure of those properties, the asserted utility of biomedical research lacks specificity. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility has not been assessed.

Claim 1 is also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.